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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/516,633	01/19/2005	David Grenville Holmes	PC/4-32514A	4568

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CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 101/2
EAST HANOVER, NJ 07936-1080

EXAMINER	
ROYDS, LESLIE A	
ART UNIT	PAPER NUMBER
1614	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/516,633	HOLMES ET AL.	
	Examiner	Art Unit	
	Leslie A. Royds	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 January 2010 and 13 April 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-7,9,11,14-16 and 18* is/are pending in the application.

4a) Of the above claim(s) *3-5 and 14-16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,6,7,9,11 and 18* is/are rejected.

7)☒ Claim(s) *6* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 3-7, 9, 11, 14-16 and 18 are presented for examination.

Applicant's Amendment filed January 28, 2010 was received and entered into the present application. Pursuant to the notice dated April 5, 2010, the reply filed January 28, 2010 was non-responsive. Applicant's amendment filed April 13, 2010 correcting these deficiencies has been received and entered into the present application.

Applicant is reminded that the instant claims are examined insofar as they read upon (i) the compound of formula (IC) as the compound of formula (I) and (ii) atherosclerosis as the condition associated with hyperlipidemia, as provided in the reply filed August 1, 2008.

Claims 1, 3-7, 9, 11, 14-16 and 18 remain pending. Claims 8, 12-13 and 19-26 are cancelled. Claims 3-5 and 14-16 remain withdrawn from consideration pursuant to 37 C.F.R. 1.142(b). Claims 1 and 9 are amended. Claims 1, 6-7, 9, 11 and 18 remain under examination.

Applicant's arguments, filed January 28, 2010 and April 13, 2010, have been fully considered. Rejections and/or objections not reiterated from previous Office Actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set of rejections and/or objections presently being applied to the instant application.

Error Noted in Claim Listing Filed April 13, 2010

Applicant is notified that the claim listing of April 13, 2010 fails to properly set forth the text of the pending claim(s) relative to the text of the immediately prior version of the claims. Specifically, Applicant has added the phrase "and/or" to l.1 of instant claim 1, striking through the phrase "and/or". However, the previous claim listing did not recite "and/or" at this position in the claim, but rather recited "and or" (see, e.g., claim 1 in the claim listing filed April 22, 2009).

Applicant is urged to comply with the provisions of 37 C.F.R. 1.121(c), which requires strikethrough or bracketing to show what has been removed from the claim and underlining to show what has been added to the claim as compared to the **immediately prior version of the claims**. Applicant is herein respectfully requested to comply with the requirements for proper claim amending as set forth in 37 C.F.R. 1.121(c) in the even that Applicant should choose to submit any subsequent claim listings to the Office. Failure to comply with 37 C.F.R. 1.121 may render future replies non-compliant.

Objection to the Claims (New Grounds of Objection)

Claim 6 is objected to for reciting a period directly following the phrase "is a compound of formula IC", which excludes the structural formula IC that is then presented as part of the claim. In order to overcome the instant objection, Applicant may wish to consider amending the claim to remove the period following the phrase "is a compound of formula IC" and adding a period directly following the structural formula IC. Applicant is reminded, however, that the adoption of such a suggestion does not necessarily equate to the obviation of any other objection and/or rejection set forth *infra*.

Claim Rejections - 35 USC § 102 (New Grounds of Rejection)

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 9 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Villhauer (U.S. Patent No. 6,166,063; 2000), already of record.

Villhauer teaches the instantly claimed compound of formula (IC) and pharmaceutical compositions thereof (abstract; col.1, l.19-31; Ex.1), wherein the acid addition salt forms of the

compound may also be used (col.1, l.19-31), which function as a dipeptidyl peptidase-IV (DPP-IV) inhibitor (col.4, l.30-32) and is disclosed for use in a method for treating conditions mediated by DPP-IV, comprising administering to a mammal in need of such treatment a therapeutically effective amount of the disclosed compound(s) or pharmaceutically acceptable acid addition salts thereof (col.4, l.19-24), wherein the condition mediated by DPP-IV includes, *inter alia*, non-insulin dependent diabetes, arthritis, obesity, osteoporosis, and other conditions related to impaired glucose tolerance (abstract).

Regarding the limitations of instant claim 9 (i.e., that LDL, Lp(a) and/or VLDL levels are lowered), though Villhauer is silent as to this effect of administering the compound of formula (IC) to a mammal (i.e., such as the mammalian subjects of Villhauer; note that the instant claims place no limitation on the mammal to be treated except that it be, simply, "a mammal"), it is noted that the teaching of administering an identical compound in an identical manner (i.e., to a mammal) must necessarily possess this same functional property of lowering LDL, Lp(a), and/or VLDL, even though such properties may not have been appreciated by the patentee at the time of the invention. This is because products of identical chemical composition cannot have mutually exclusive properties when used in the same manner because a chemical compound and its properties are inseparable. Thus, if the prior art teaches the apparently identical chemical structure, particularly for use in the same manner, the properties Applicant discloses and/or claims must necessarily be present, absent factual evidence to the contrary.

In re Best (195 USPQ 430) and *In re Fitzgerald* (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter, which there is reason to believe includes functions and/or properties that are newly cited, or is identical to a product instantly claimed. In such a situation the burden is shifted to the Applicants to "prove that subject matter to be shown in the prior art does not possess the characteristic relied on" (205 USPQ 594, second column, first full paragraph). There is no requirement that a person of ordinary skill in the art would have recognized the newly cited function and/or property at the time of invention, so long as the function and/or property can be demonstrated to be

reasonably expected to be present. *Schering Corp. v. Geneva Pharm. Inc.*, 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2003); see also *Toro Co. v. Deere & Co.*, 355 F.3d 1313, 1320, 69 USPQ2d 1584, 1590 (Fed. Cir. 2004) ("[T]he fact that a characteristic is a necessary feature or result of a prior-art embodiment (that is itself sufficiently described and enabled) is enough for inherent anticipation, even if that fact was unknown at the time of the prior invention"). In the instant case, though Villhauer may not expressly teach the function of the compound of formula (IC) for lowering LDL, Lp(a) and/or VLDL, the prior art to Villhauer teaches the identical compound as that presently claimed for administration in the same manner to an identical host (i.e., a "mammal"), and, therefore, these resultant properties must also be the same, absent factual evidence to the contrary. The burden is now shifted to Applicant to prove that, in fact, Villhauer does not possess these same claimed characteristics.

Note that the instant rejection is necessitated by Applicant's amendment to instant claim 9 removing the phrase "and another active agent". In light of the instant specification, the "active agent" originally provided for in instant claim 9 to be used with the compound of formula (IC) circumscribed the use of other "active agents" that possessed pharmaceutical activity other than what would have been observed from a pharmaceutically acceptable carrier or diluent as provided for in Villhauer. In other words, Villhauer was not previously applied under 35 U.S.C. 102(b) because it did not provide for combination therapy with "another active agent" with clear pharmaceutical activity (i.e., not simply a carrier or diluent as taught in Villhauer. For these reasons, this new rejection is applied as a result of Applicant's amendment to the claims.

Claim Rejections - 35 USC § 103 (New Grounds of Rejection)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 6-7 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Villhauer (U.S. Patent No. 6,166,063; 2000) in view of Luskey et al. (U.S. Patent No. 6,262,118; 2001), each already of record.

Note that the instant rejection is substantially equivalent to the previous rejection set forth under 35 U.S.C. 103(a) but is modified due to the fact that the instant claims no longer provide for combination therapies comprising the instantly claimed compound of formula (IC) with an antihyperlipidemic agent. For this reason, the instant rejection is necessitated by Applicant's amendment to the instant claims cancelling those claims directed to combination therapies.

Villhauer teaches the instantly claimed compound of formula (IC) and pharmaceutical compositions thereof (abstract; col.1, l.19-31; Example 1), wherein the acid addition salt forms of the compound may also be used (col.1, l.19-31), which function as a dipeptidyl peptidase-IV (DPP-IV) inhibitors (col.4, l.30-32) and is disclosed for use in a method for treating conditions mediated by DPP-IV, comprising administering to a mammal in need of such treatment a therapeutically effective amount of the disclosed compound(s) or pharmaceutically acceptable acid addition salts thereof (col.4, l.19-24), wherein the condition mediated by DPP-IV includes, *inter alia*, non-insulin-dependent diabetes, arthritis, obesity, osteoporosis, and other conditions related to impaired glucose tolerance (abstract).

Villhauer et al. fails to specifically teach the treatment of patients in need of treatment of hyperlipidemia and/or atherosclerosis (claims 1 and 7).

Luskey et al. teaches that the premature development of atherosclerosis and hyperlipidemia are characteristic features of patients with diabetes and that, specifically, hyperlipidemia is a precipitating factor for this disease (col.2, l.1-8).

In view of such teachings, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention that the disclosed DPP-IV inhibitor of formula (IC) of Villhauer for the treatment of diabetes would have been reasonably expected to exert the same or substantially equivalent efficacy in the treatment of hyperlipidemia and/or atherosclerosis in a patient in need of such treatment because: (1) the compound of Villhauer was known to have efficacy in treating patients that suffer from diabetes *per se* and (2) patients that have diabetes also suffer from premature development of atherosclerosis and hyperlipidemia that precipitate the development of diabetes, as evidenced by Luskey et al. Villhauer provides the clear teaching that the instantly claimed compound of Formula (IC) is, in fact, effective for treating all diabetes patients, i.e., 100% of patients with diabetes, without exclusion. Of this entire population of diabetes patients, Luskey et al. provides the factual extrinsic evidence demonstrating that a subpopulation of diabetes patients also suffers concomitantly from atherosclerosis and/or hyperlipidemia. Accordingly, the suggestion of Villhauer to use the claimed compound of Formula (IC) for treating any diabetes patient is a clear suggestion to use it in any subpopulation of diabetes patients, such as those patients also suffering from concomitant atherosclerosis and/or hyperlipidemia, with the reasonable expectation of the same (or at least substantially equivalent) level of efficacy in treating this subpopulation of patients with atherosclerosis and/or hyperlipidemia as would be expected in the treatment of diabetes patients *per se*. Furthermore, since products of identical composition cannot have mutually exclusive properties when administered under identical conditions, or, as in the present case, the same host, whatever effect(s) the instantly claimed compound of Formula (IC)

has in treating atherosclerosis and/or hyperlipidemia must necessarily be present in the method disclosed by Villhauer, absent factual evidence to the contrary.

Response to Applicant's Arguments

Applicant traverses the instant rejection, stating that it would not have been obvious to one of skill in the art to combine the teaching of Villhauer (i.e., that the compound of Formula (I) treats diabetes) with Luskey (i.e., that derivatives of halofenic acid can be used to treat hyperlipidemia). Applicant opines that the references, alone or in combination, contain no teaching, suggestion or motivation to use the compound of Formula (I) to treat hyperlipidemia.

Applicant's traversal has been fully and carefully considered, but fails to be persuasive.

In the instant case, Villhauer clearly teaches that the compound of formula (IC) is an efficacious therapy for the treatment of patients with diabetes, i.e., 100% of patients with diabetes, without exclusion. Luskey et al. provides the extrinsic evidence to demonstrate that, within the population of diabetic patients *per se*, there are clearly patients within this population that also suffer from hyperlipidemia and/or atherosclerosis, because, as evidenced by Luskey et al., there is a clear correlation between premature development of atherosclerosis and hyperlipidemia in patients with diabetes. In other words, the cited prior art clearly establishes that there is a patient population that exists in the diabetic population that is both (a) diabetic and (b) suffering from hyperlipidemia and/or atherosclerosis. Accordingly, of the diabetic population treatable via the method Villhauer, there are patients within this population that also suffer from hyperlipidemia and/or atherosclerosis and, thus, the practice of administering the compound of formula (IC) to *any* diabetic patient would also, therefore, circumscribe its practice in a diabetic patient that also suffers from hyperlipidemia and/or atherosclerosis, which is a subpopulation clearly described by Luskey et al. The motivation and/or reasonable expectation of success is derived directly from the teachings of Villhauer, who explicitly teaches the administration of the compound of formula (IC) to *any*

diabetic patient, i.e., patients with diabetes that may or may not also be suffering from a concomitant disorder, for the purpose of treating diabetes, which is clear motivation to administer the compound of formula (IC) to any diabetic patient, including any subpopulation of diabetic patients thereof, which, as evidenced by Luskey et al., clearly circumscribes the treatment of diabetic patients who also suffer from hyperlipidemia and/or atherosclerosis, absent factual evidence to the contrary. As a result, Applicant's argument that the cited prior art contains no teaching, suggestion or motivation to use the compound of Formula (I) to treat hyperlipidemia is clearly unpersuasive in establishing nonobviousness of the instant claims.

For these reasons *supra*, rejection of claims 1, 6-7 and 11 is proper.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 6-7, 9, 11 and 18 remain provisionally rejected on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claims 6 and 9 of copending U.S. Patent Application No. 11/815,536; or claim 6 of copending U.S. Patent Application No. 11/868,129, each already of record, for the reasons of record set forth at p.8-9 of the previous Office Action dated August 31, 2009, of which said reasons are herein incorporated by reference.

Claims 1, 6-7, 9, 11 and 18 remain provisionally rejected on the grounds of nonstatutory

obviousness-type double patenting as being unpatentable over claims 5-6, 8 and 16 of U.S. Patent Application No. 11/576,860; or claims 9, 12-19 and 20-26 of U.S. Patent Application No. 11/577,941; or claims 1, 16-18 and 34 of U.S. Patent Application No. 11/628,546; or claims 5-7, 13-14 and 18 of U.S. Patent Application No. 12/067,822, each alternatively in view of Luskey et al. (U.S. Patent No. 6,262,118; 2001) and citing to STN Registry No. 274901-16-5 as evidence, each already of record, for the reasons of record set forth at p.11-17 of the previous Office Action dated August 31, 2009, of which said reasons are herein incorporated by reference.

Cancellation of claims 8, 12-13 and 19-26 renders the instant rejections moot against such claims.

Note that U.S. Patent Application Nos. 11/497,130 and 10/579,580 have each been abandoned and, therefore, the provisional rejections over the '130 and the '580 applications are moot.

Response to Applicant's Arguments

Applicant states in the remarks dated April 13, 2010 that the filing a Terminal Disclaimer will be considered pending the identification of allowable subject matter. Note that Applicant specifically acknowledges the rejections over the '536 or the '130 application(s).

In the absence of any remarks regarding the propriety of the instant rejection and/or the filing of a Terminal Disclaimer and/or the identification of allowable subject matter in the instant or copending applications, the rejections remain proper for the reasons of record set forth at p.8-9 and p.11-17 of the previous Office Action dated August 31, 2009.

Note that the remarks set forth with regard to the '536 and '130 applications are understood to apply to each of the cited provisional rejections over the other copending applications though not specifically stated in Applicant's remarks. Applicant is notified, however, that a failure to acknowledge *each and every* obviousness-type double patenting rejection in future replies will render the reply non-

compliant and notice to that effect will be sent, which may delay prosecution.

For these reasons *supra*, and those previously made of record at p.8-9 and p.11-17 of the Office Action dated August 31, 2009, rejection of claims 1, 6-7, 9, 11 and 18 is proper.

Conclusion

Rejection of claims 1, 6-7, 9, 11 and 18 is proper.

Claims 3-5 and 14-16 remain withdrawn from consideration pursuant to 37 C.F.R. 1.142(b).

No claims of the present application are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leslie A. Royds whose telephone number is (571)-272-6096. The examiner can normally be reached on Monday-Friday (9:00 AM-5:30 PM).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571)-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Leslie A. Royds/
Primary Examiner, Art Unit 1614

July 12, 2010